

## ABSTRACT OF THE DISCLOSURE

Fc fusion proteins of human EPO with increased biological activities relative to rHuEPO on a molar basis are disclosed. The HuEPO-L-vFc fusion protein comprises HuEPO, a flexible peptide linker of about 20 or fewer amino acids, and a human IgG Fc variant. The Fc variant is of a non-lytic nature and shows minimal undesirable Fc-mediated side effects. A method is also disclosed to make or produce such fusion proteins at high expression levels. Such HuEPO-L-vFc fusion proteins exhibit extended serum half-life and increased biological activities, leading to improved pharmacokinetics and pharmacodynamics, thus fewer injections will be needed within a period of time.